

## REMARKS

Claims 30, 35-39 and 43-59 are presently pending in this application. In the present Amendment, Applicants have amended claims 30, 39, 44, 47, 56 and 59. Therefore, claims 30, 35-39 and 43-59 are under consideration upon entry of the present amendment. No new matter was added to the application by way of the present Amendment.

### Objections to the Specification

The Examiner objected to the Abstract of the disclosure, as the Abstract exceeded the limit of 150 words, as set forth in MPEP § 608.01(b). Applicants have amended the Abstract herein so that the Abstract contains fewer than 150 words. Accordingly, Applicants respectfully submit that the Examiner's objection has been obviated.

The Examiner has also objected to the disclosure for not containing a heading before the brief description of the drawings. Applicants have herein amended page 11 of the specification to include the heading, "Brief Description of the Drawings." immediately prior to the brief description of the drawings. Accordingly, Applicants respectfully submit that the Examiner's objection has been overcome. No new matter has been added by way of the amendments to the specification.

### Claim Objections

The Examiner objected to claim 30 for improper claim dependence in subpart (d). Applicants have amended claim 30 herein such that subpart (d) properly depends from subparts (a) to (c).

The Examiner objected to claims 47 and 56 for improper capitalization of the word "the." Applicants have amended claims 47 and 56 herein such that the word "the" is properly capitalized in all instances.

The Examiner also objected to claim 29 for recitation of the acronym "STRE" without preceding introduction as to what the acronym represents. Applicants respectfully point out that claim 29 is not currently pending, and was canceled by way of the Preliminary Amendment submitted in conjunction with this application on October

31, 2001. Insofar as the Examiner's rejection applies to pending claim "39," Applicants have amended claim 39 herein to include the term "Stress Responsive Element" prior to the acronym STRE.

Applicants respectfully submit that all of the Examiner's objections to the claims have either been overcome or no longer apply. No new matter has been added by way of the amendments to the claims.

#### Sequence Compliance

The Examiner noted that the present application contains nucleic acid sequences not identified by unique SEQ ID NO: sequence identifiers. Specifically, the Examiner pointed out that Figure 5, which depicts a sequence alignment of five nucleic acid sequences, contains sequences not identified in the specification by way of a sequence identifier.

Applicants have herein amended the description of Figure 5 in the Brief Description of the Drawings such that now, each of the five sequences depicted in Figure 5 is properly referred to by way of a sequence identifier. Specifically, the *S. cerevisiae* sequence is SEQ ID NO:29, the *K. lactis* sequence is SEQ ID NO:30, the *C. albicans* sequence is SEQ ID NO:31, the *S. pombe* sequence is SEQ ID NO:32 and the *A. niger* sequence is SEQ ID NO:33.

Applicants also submit herewith an amended version of the sequence listing that contains SEQ ID NOS:29-33. The sequence listing is being provided both as a paper copy and in computer-readable format, and is being submitted in conjunction with a Verified Statement indicating that the paper and computer-readable versions are identical and do not add new matter to the application. Accordingly, Applicants respectfully submit that the present application is in full compliance with the requirements of 37 C.F.R. § 1.821 through 1.825.

#### Rejection of Claim 59 under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claims 30 and 59 under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, it is the Examiner's view that the claims lack proper antecedent basis.

With respect to claim 30, the Examiner states that the recitation of the phrase “a nucleic acid” in subpart (a) does not find proper antecedent basis in the preamble of the claim, and in particular, in the phrase, “An isolated nucleic acid molecule comprising a heat inducible promoter...” The Examiner also suggests that the amendment of subpart (a) to recite the phrase “the nucleic acid” would be remedial. Applicants respectfully disagree for the following reasons and submit that claim 30 is not indefinite.

Applicants point out that subpart (a) of the claim recites “a nucleic acid sequence” that defines a promoter structure that is a part of the “isolated nucleic acid molecule” of the claim. Thus, “a nucleic acid sequence” as recited in subparts (a)-(c) can be distinguished from “An isolated nucleic acid molecule” as recited in the preamble of the claim. “A nucleic acid sequence” as set forth in subpart (a) is only one of six members of a Markush group set forth in claim 30 subparts (a), (b), (c), (d), (e) and (f).

The requirements for proper antecedent basis are set forth in MPEP § 2173.05(e). This section of the MPEP provides, in part, that a claim may be indefinite “when it contains words or phrases whose meaning is unclear.” By way of example, MPEP § 2173.05(e) sets forth that a lack of clarity “could arise where a claim refers to ‘said lever’ or ‘the lever,’ where the claim contains no earlier recitation or limitation of a lever and where it would be unclear as to what element the limitation was making reference.” Applicants submit that subpart (a) of claim 30, “a nucleic acid sequence comprising the promoter sequence of a *Hansenula polymorpha* gene encoding a protein having trehalose-6-phosphate synthase activity,” was not earlier recited or presented as a limitation in the preamble of claim 30. Rather, the nucleic acid sequence set forth in subpart (a) was presented for the first time in subpart (a), and properly claims “a” nucleic acid sequence.

MPEP § 2173.05(e) also provides, in part, that a claim is not per se indefinite if the body of the claim recites additional elements which do not appear in the preamble. Specifically, this section states:

**The mere fact that the body of a claim recites additional elements which do not appear in the claim’s preamble does not render the claim indefinite under 35 U.S.C. 112, second paragraph. See In re Larsen, No. 01-1092 (Fed. Cir. May 9, 2001) (unpublished) (The preamble of the Larsen claim recited only a hanger and a loop but the**

body of the claim positively recited a linear member. The examiner rejected the claim under 35 U.S.C. 112, second paragraph because the omission from the claim's preamble of a critical element (i.e., a linear member) renders that claim indefinite. The court reversed the examiner's rejection and stated that the totality of all the limitations of the claim and their interaction with each other must be considered to ascertain the inventor's contribution to the art. Upon review of the claim in its entirety, the court concluded that the claim at issue apprises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, paragraph 2.). (emphasis added).

Accordingly, Applicants respectfully submit that the Examiner's indefiniteness rejection of claim 30 is improper and respectfully request withdrawal of the rejection.

The Examiner also rejected claim 59 as indefinite for recitation of the term "a heat-inducible promoter" in subpart (a). While not acquiescing to the Examiner's rejection, but in an attempt to expedite prosecution of the application, Applicants have herein amended claim 59 to recite "the heat-inducible promoter" in subpart (a) of the claim. Accordingly, Applicants respectfully submit that the Examiner's rejection has been overcome and respectfully request withdrawal of the rejection.

Rejection of Claims 30, 35-39 and 43-49 under 35 U.S.C. § 112, First Paragraph  
("Written Description")

The Examiner rejected claims 30, 35-39 and 43-49 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed (a "written description" rejection). In particular, the Examiner rejects the claim language drawn to nucleic acid molecules that "hybridize" with the complementary strand of the promoter sequences of the H. polymorpha gene encoding TSP because, in the Examiner's view, the specification does not provide "a representative number of species sufficient to convince the skilled artisan that the applicant is in possession of the claimed genus."

It is apparently the Examiner's view that the disclosure only provides a "single species" that satisfies the written description requirement, and that the disclosure is solely to one set of stringent hybridization conditions. Applicants respectfully disagree, and remind the Examiner that the written description requirement may be satisfied by the presentation of a "representative number of species" of a genus, and that a

representative number of species may even be a single species where the skill in the relevant art and the predictability of the art is adequate, such as in the art of nucleic acid hybridization. (Guidelines for Examination of Patent Applications Under the 35 U.S.C. § 112, ¶ 1, “Written Description” Requirement, Federal Register, Vol. 66, No. 4, Friday, January 5, 2001, page 1106). Satisfactory disclosure of a “representative number” depends on whether one of skill in the art would recognize that the applicant was in possession of the *necessary common attributes or features* of the elements possessed by the members of the genus in view of the species disclosed. (Id.).

Applicants submit that a common feature of any stringent hybridization conditions that are based on the hybridization conditions set forth in amended claim 30 include the manipulation of salt and/or temperature parameters of the hybridization conditions. This common feature is clearly set forth on page 4 of the instant application, where Applicants provide several non-limiting examples of stringent hybridization conditions varying in salt and/or temperature conditions, and would therefore be readily understood by one of skill in the art. For example, Applicants set forth in the first paragraph at the top of page 4 in the specification that stringent hybridization conditions include, but are not limited to, hybridization at 68°C in 2x SSC buffer (sodium chloride/sodium citrate buffer, pH 7.0).

While not necessarily agreeing with the Examiner’s reasoning, but in an attempt to expedite prosecution of the present application, Applicants have amended claim 30 herein to include specific stringent hybridization conditions. Specifically, Applicants have amended subpart (c) to read, “a nucleic acid which hybridizes, under stringent hybridization conditions, with the complementary strand of the nucleic acid set forth in one of (a) or (b), wherein said stringent hybridization conditions comprise (i) incubation of said nucleic acid set forth in one of (a) or (b) in 7% sodium dodecyl sulfate, 1% bovine serum albumin, 1 mM ethylenediaminetetraacetic acid, in 250 mM sodium phosphate buffer at pH 7.2 at 65°C overnight, followed by washing with sodium chloride/sodium citrate buffer pH 7.0 (2x SSC), 0.1% sodium dodecyl sulfate, or (ii) incubation of said nucleic acid set forth in one of (a) or (b) in 2x SSC at 68°C.” Support for the amendments to claim 30 is found on page 4 of the specification, in the first paragraph at the top of the page. Therefore, because the amendments to claim 30 are

fully supported in the specification as filed, the amendments to claim 30 add no new matter.

The Examiner has also rejected claims 44-46 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed. In particular, the Examiner rejects the claim language drawn to nucleic acids having 80% identity to the nucleic acid sequence set forth in SEQ ID NO:6, as well as polypeptide fragments of the polypeptide sequence set forth in SEQ ID NO:7.

While not necessarily agreeing with the Examiner's reasoning, Applicants have herein amended claim 44, from which claims 45 and 46 depend, such that claim 44 no longer recites "percent identity" or "fragment" language. Specifically, Applicants have amended claim 44 to recite a nucleic acid sequence comprising SEQ ID NO:6, a nucleic acid sequence having the amino acid sequence indicated in SEQ ID NO:7, and a nucleic acid sequence which encodes a polypeptide having an amino acid sequence comprising SEQ ID NO:7. Support for the amendments to claim 44 can be found throughout the specification, and in particular, in Experimental Examples 1, 2, 3 and 4. Therefore, because the amendments to claim 44 are fully supported in the specification as filed, the amendments to claim 44 add no new matter.

Applicants submit that amended claim 30, and claims 35-39 and 43-49, which depend either directly or indirectly from claim 30, satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. Further, amended claim 44, and claims 45 and 46, which depend from claim 44, also satisfy the written description requirement. Accordingly, Applicants respectfully submit that the Examiner's written description rejection has either been overcome or no longer applies, and request reconsideration and withdrawal of the rejection.

#### Rejection of claims 44-46 under 35 U.S.C. § 112, first paragraph ("Enablement")

The Examiner has rejected claims 44-46 under 35 U.S.C. § 112, first paragraph, because in the Examiner's view, the specification, while being enabling for full length H. polymorpha trehalose-6-phosphate synthase, does not reasonably provide

enablement for sequences with 80 or 90 percent identity, or partial sequences of trehalose-6-phosphate. Applicants respectfully submit that the amendments made to claim 44 in response to the Examiner's written description rejection, as set forth in detail above, render the Examiner's enablement requirement moot.

The factors to be considered in determining whether undue experimentation is required to practice an invention have been set forth in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988) and include the quantity of experimentation necessary, the amount of guidance or direction presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative level of skill in the art, the predictability or unpredictability of the art and the scope of the claims.

In view of the above-described amendments to claim 44, Applicants respectfully submit that it would not be undue experimentation for the skilled artisan, when armed with the present disclosure, to practice the claimed invention. The specification provides abundant guidance, by way of working examples in the specification (see Experimental Examples 1, 2, 3 and 4), for the practice of the claimed invention. Further, Applicants submit that the amendments and arguments made in response to the Examiner's written description rejection, set forth in detail above, apply with equal force to the Examiner's enablement rejection of claims 44-46.

Therefore, Applicants respectfully submit that the Examiner's enablement rejection under 35 U.S.C. § 112, first paragraph, has either been overcome or rendered moot, and respectfully request reconsideration and withdrawal of the rejection.

#### Rejection Under 35 U.S.C. § 102(b)

The Examiner rejected claim 30 under 35 U.S.C. § 102(b), as being anticipated by Xiao-Dong et al. ("the Liu reference"). The Examiner's rejection appears to be based on subsection (c) of claim 30, which, in the Examiner's view, is drawn to "any sequence capable of hybridizing, even if just momentarily," to the promoter of an H. polymorpha gene having trehalose-6-phosphate activity.

It is well settled that "[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a

single prior art reference." MPEP §2131 (quoting *Verdegaal Bros. v. Union Oil Co. of Calif.*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)). "The identical invention must be shown in as complete detail as is contained in the . . . claim." *Id.* (quoting *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)). Therefore, in order for a rejection under 35 U.S.C. § 102(b) to be proper, each and every element of Applicants' invention must be disclosed by the Xiao-Dong reference.

As described above in response to the Examiner's written description rejection of claim 30, Applicants have amended claim 30 herein to recite specific hybridization conditions. Therefore, subpart (c) of amended claim 30 requires that a nucleic acid of the claimed invention must hybridize with the nucleic acids set forth in either one of subparts (a) or (b) of the claim, under stringent conditions, in order to fall within the scope of claim 30. However, the Xiao-Dong reference does not disclose any such nucleic acids encompassed by claim 30. Specifically, the Xiao-Dong reference does not specifically disclose a nucleic acid that can hybridize, under the stringent hybridization conditions set forth in subpart (c) of claim 30, to a nucleic acid sequence comprising the promoter sequence of a *Hansenula polymorpha* gene encoding a protein having trehalose-6-phosphate synthase activity, or to a nucleic acid having the sequence set forth in SEQ ID NO:1, as set forth in subparts (a) and (b).

Therefore, Applicants submit that Xiao-Dong does not anticipate amended claim 30. Accordingly, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. § 102(b) no longer applies, and respectfully request reconsideration and withdrawal of the rejection.

Summary

Applicants respectfully submit that each of the Examiner's objections and rejections has either been overcome or rendered moot, and that each of claims 30, 35-39, and 43-59 is fully supported by the specification as originally filed and in condition for allowance. Consideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,

**ROMANO ET AL.**

MAY 7, 2004  
(Date)

By: Kathryn Doyle  
KATHRYN DOYLE  
Registration No. 36,317  
MORGAN, LEWIS & BOCKIUS, LLP  
1701 Market Street  
Philadelphia, PA 19103-2921  
Telephone: (215) 963-5000  
Direct Dial: (215) 963-4723  
Facsimile: (215) 963-5299  
E-Mail: [kdoyle@morganlewis.com](mailto:kdoyle@morganlewis.com)  
Attorney for Applicants

KD/TMS *del*

Enclosures: (Sequence Listing Paper Copy, Sequence Listing Computer Readable Format, Verified Statement of the Sequence Listing)